

REMARKS

Claims 1 to 25 are in the application. Claims 1, 14, 18, and 23 have been amended. No new matter is believed added. Claims 14 and 23 have been updated with each respective US publication or patent number where applicable.

Rejection under 35 USC § 112, first paragraph

The specification is objected to under 35 USC § 112, first paragraph as failing to adequately teach how to make and/or use the invention, and thereby failing to provide an enabling disclosure. Applicants respectfully traverse this objection.

Claims 1 to 13 and 18 to 22 are rejected under 35 USC § 112, first paragraph for the reasons set forth in the objection to the specification.

Claims 14 and 23 are rejected under 35 USC § 112, first paragraph as based on a disclosure which is not enabling. Applicants also respectfully traverse these rejections.

The Examiner indicates that Applicant fails to set forth the criteria that defines “neither those compounds possessing CSBP/p38 inhibitor activity useful for treating those viral diseases herein envisioned, nor a method for ascertaining compounds possessing this activity absent an individual assay of compounds. Additionally, Applicant fails to provide information allowing the skilled artisan to ascertain these compounds without undue experimentation”.

Applicants draw the Examiners attention to the Background of the Invention section which describes and cites to a number of references studies of rhinoviruses, and the linkage of such an infection to increased intranasal levels of kinins, IL-1, IL-8, IL-6, IL-11, etc. (page 1, lines 28-36).

Applicants provide in their Brief Description of the Drawings 7 Figures with data as demonstrated in their Methods Section of the specification. The Methods section starts on page 12, lines 26 to end of the specification and runs through page 17, lines 1 to 28. This section describes in great detail the various cell lines used in the experiment (page 12, lines 27 to end, and page 13, lines 1 to 14. Use of influenza virus strains instead of rhinovirus cell lines is described on page 13, lines 15 to 14. Inoculation procedures are on page 13, lines 24 to 31. Virus titration levels are described on page 13, lines 32 to end, and on page 14, lines 1 to 4. Cytokine levels were measured in an Elisa assay and are described on page 14, lines 4 to 8. A myeloperoxidase activity assay is described on page 14, lines 9 to 22. A whole Body Plethysmography assay is described on page 14, lines 23 to 34. Determination of arterial oxygen saturation is described on page 14, lines

35 and 36 and on page 15, lines 1 and 2. Results are shown on page 15, lines 4 to end and on page 16, lines 1 to 10. P38 Activation and Effects on in vitro influenza virus infection are taught on page 16, lines 11 to end. *In-vivo* effects for p38 inhibitors is shown on page 17, lines 1 to 28. A number of these results are demonstrated in the accompanying before mentioned figures.

It should be noted that in the *in-vivo* effects for p38 inhibitor section, five independent studies, not just one experiment, demonstrates the claimed results herein. More than one compound has been tested and shown effective in this assay.

In the RESULTS section, inhibition of cytokine production is established by a number of different inhibitors, including an inactive analogue. The results demonstrate that concentrations of the cytokines were lower in infected cells treated with p38 inhibitors than those from untreated, and infected cultures. The compounds did not exhibit a direct antiviral activity (page 16, lines 7 to 10).

With respect to the Examiners comments, it is believed that the instant application first, clearly teaches how to determine which compounds are p38 inhibitors. This is an art recognized assay, and is shown and described in the man patents and applications noted on page 5, lines 12 to 36. Secondly, the specification teaches how to conduct the necessary experimentation to determine if a compound is useful for treating the inflammation associated with the described viral diseases. Thirdly, in direct contrast to the Examiners comments, there are several methods (art recognized) taught to ascertain the claimed activity. It is not believed that this is "undue experimentation" as Applicants have demonstrated that inhibition of cytokines associated with certain viral diseases can be influenced in a positive manner by compounds, which are inhibitors of these cytokines. Once Applicants have demonstrated this correlation, as in Applicants specification, use of a p38 inhibitor in this method would be expected to useful for treating an individual infected by such viral organisms.

The Examiner comments that the "pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity". While this is a generalised statement, it is believed that Applicants have supplied more than a sufficient nexus, with differing classes of compound, for the underlying mechanism of action by p38 inhibitors. The testing of such compounds, for p38 inhibition, is also well established in the art. Once you know a compound has such activity, depending upon its potency, you will be able to influence to a lesser or greater extent the inflammation associated with a viral infection in a mammal. More than sufficient information is

presented to practice the claimed invention, and does not require undue experimentation to do so.

With respect to the Examiners rejection of Claim 14 and 23 being based up on a disclosure which is not enabled is unclear. The various methods and assays necessary for determination of p38 inhibition is already well known in the art prior to the filing of this application. The listing of patents and application, as shown on page 5, lines 12 to 36 is for inclusion of classes of compounds which are all described in the art as p38 inhibitors. Applicants do not need to incorporate such for essential material. It is merely a short hand method for describing and claiming compounds useful in the present invention. However, to advance prosecution Applicants will amend claims 14 and 23 to delete the so noted WO applications which do not have a published US application number or corresponding US patent. Applicants reserve their right to file continuation or divisional application on such cancelled or deleted subject matter.

Consequently, reconsideration and withdrawal of the rejection to the claims is respectfully requested.

Rejection under 35 USC § 112, second paragraph

Claims 1 to 13, and 18 to 22 are rejected under 35 USC §112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. Applicants respectfully traverse this rejection.

The Examiner states that the phrase “compounds possessing CSBP/p38 inhibitor” is indefinite. Applicants have incorporate by reference a number of US patents which clearly teach the skilled artisan the assay methods by which one can determine if a compound is an inhibitor of the CSBP kinase. At the time of filing of this application this is a well known, art recognized kinase, and methods for determining such are in the public domain. The assay is not an undue burden, nor requires extensive experimentation to determine if a compound possesses such activity.

However, Applicants are unclear wherein the claims such as phrase exists as stated by the Examiner. Clarification with particularity is requested so that Applicants may respond accordingly. Claim 1 clearly states an “effective amount of a CBSP/p38 inhibitor” and not a compound possessing such activity.....

Applicants respectfully request reconsideration and withdrawal of the rejection to the claims under 35 USC §112, second paragraph.

Rejection under 35 USC §102

Claims 1 to 6, 10 and 14 are rejected under 35 USC §102(b) as being anticipated by Adams et al. ('644).

Claims 18, 21, 23, and 25 are rejected under 35 USC §102(b) as being anticipated by Adams et al. ('644) in view of the Merck Manual. Applicants respectfully traverse these rejections.

The Examiner states that page 1000 of the Merck Manual "teaches the general incapacitating nature of influenza, and those complications here envisioned as collateral to this malady." Applicants respectfully disagree that this is the teaching as presented on page 1000 of the Merck Manual. As the prior pages of the Manual are not presented in this rejection, it is unclear what on page 1000 the Examiner is referring to. There is a small box describing "Complications of Influenza" and in the Prevention section a short discussion of vaccination and treatment with known antiviral drugs.

The Adams et al. patent, US 5,656,644, cited in Applicants specification on page 5, line 15 are suitable compounds for use as p38 inhibitors. The Examiner does not, however, teach how the compounds as shown in the '644 patent relate to the Prevention section of the Merck Manual. Clarification is respectfully requested.

Applicants have amended Claim 1 and 18 to more particularly point out and distinctly claim the invention as described herein. Applicants reserve their right to file divisional or continuation applications on the cancelled or deleted subject matter.

The '644 patent does not describe treatment of the common cold, or respiratory viral infection caused by human rhinovirus (HRV), or other enteroviruses, coronavirus or respiratory syncytial virus by the p38 inhibitors noted therein. Therefore, Claim 1 is not anticipated by the teachings of the '644 patent. The rejection is not remedied by the disclosure of the Merck Manual. Claim 18 is directed to influenza induced pneumonia (Claim 18) as a complication of influenza. This is not taught by the '644 patent, and the Merck Manual does not remedy this lack of disclosure.

Consequently, withdrawal of the rejection to Claims 1 to 6, 10 and 14, as well as claims 18, 21, 23 and 25 under 35 USC §102(b) is respectfully requested.

Rejection under 35 USC §103

Claims 1 to 7, 10, 14 to 16, 18, 21 and 23 to 25 are rejected under 35 USC §103 as being unpatentable over Adams et al. patents in view of the Merck Manual.

Applicants respectfully traverses this rejection.

The Examiner cites three US Patents of Adams et al., (US 5,756,499; US 5,593,992 and US 5,656,644) as well as a WO application (WO 97/25048). All four of these references are cited in Applicants specification, page 5, lines 12 to 35. The Examiner cites the teachings of the Merck Manual to remedy the lack of recitation in the above patents for the specific compounds of claim 15 and 24, and for the recitation of the symptomology collateral to an influenza infection.

The Examiner also states that “the claims are directed to treating a disease with old and well known compounds or compositions”. The specification can not be rejected as nonenabling under 35 USC §112 for failing to provide information about such old and well known compounds and then be rejected under 35 USC §103 for claiming such “old and well known compounds” in another use. This is an inconsistent rejection.

The above noted Adams et al. patents and application all disclose compounds which have p38 inhibitory activity. These compounds, along with the others cited in claims 18, etc. have the required activity, that of inhibition of the p38 kinase which is necessary for treatment of the inflammation associated with the claimed viral infections herein.

The Adams et al. patents and WO application do not disclose treatment of the common cold, or respiratory viral infection caused by human rhinovirus (HRV), or other enteroviruses, coronavirus or respiratory syncytial virus by the p38 inhibitors noted therein. This failure is not remedied by the disclosure of the Merck Manual. The Merck Manual does not direct the skilled artisan to treatment of a human afflicted with these other viral organisms. The present invention demonstrates that p38 inhibitors can be useful for such infections. The Adams et al. patents do not disclose treatment of influenza induced pneumonia by p38 inhibitors and this failure is also not remedied by the disclosure of the Merck Manual.

Therefore, in view of this reconsideration and withdrawal of the rejection to the claims under 35 USC §103 is respectfully requested.

Rejection under 35 USC §103

Claims 8, 9, 11, 12, 13, 19, 20 and 22 are rejected under 35 USC §103 as being unpatentable over Adams et al. patents in view of the Merck Manual as set forth in the prior rejection, further in view of Wilkowski et al. patents. Applicants respectfully traverses this rejection.

For the reasons stated above and incorporated herein, the Adams et al. patents do not disclose treatment of inflammation associated with the common cold or respiratory viral infections caused by human rhinovirus, other enteroviruses, coronavirus or respiratory syncytial virus. The Merck Manual does not remedy this failure to disclose these particular viral infections. The inclusion of the Wilkowski et al. patents does not provide any additional teachings which suggest the use of p38 compounds in this therapy.

Therefore, in view of these remarks, reconsideration and withdrawal of the rejection to the claims under 35 USC §103 is respectfully requested.

Rejection under 35 USC §103

Claim 17 is rejected under 35 USC §103 as being unpatentable over Adams et al. patents, in view of the Merck Manual as set forth above for claims 1 to 7, 10, 14 to 16, 18, 21, and 23 to 25, further in view of Bemis et al patent. Applicants respectfully traverses this rejection.

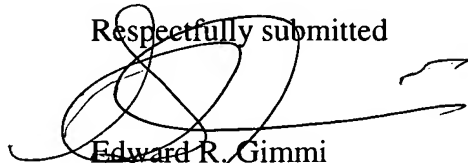
For the reasons stated above and incorporated herein, the Adams et al. patents do not disclose treatment of inflammation associated with the common cold or respiratory viral infections caused by human rhinovirus, other enteroviruses, coronavirus or respiratory syncytial virus. The Merck Manual does not remedy this failure to disclose these particular viral infections. The inclusion of the Bemis et al. patent does not provide any additional teachings which suggest the use of p38 compounds in this therapy.

Therefore, in view of these remarks, reconsideration and withdrawal of the rejection to the claims under 35 USC §103 is respectfully requested.

Should the Examiner have any questions or wish to discuss any aspect of this case, the Examiner is encouraged to call the undersigned at the number below. It is not believed that this paper should cause any additional fees or charges to be required, other

than expressly provided for already. However, if this is not the case the Commissioner is hereby authorized to charge Deposit Account 19-2570 accordingly.

Respectfully submitted

A handwritten signature in black ink, appearing to be 'Edward R. Gimmi', written over the typed name.

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